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Central fatigue is greater than peripheral fatigue in people with joint hypermobility syndrome

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ABSTRACT

Purpose: People with Joint Hypermobility Syndrome (JHS) suffer with fatigue. The purpose of this project was to investigate the contribution of central and peripheral fatigue.
Methods: Electrical stimulation of the musculocutaneous nerve to biceps brachii, and transcranial magnetic stimulation over the motor cortex supplying biceps brachii were used. Peripheral and central fatigue were assessed during a control, fatiguing and recovery phase protocol.
Results: JHS participants perceived greater fatigue during the protocol compared to a control group and did not recover. Central and peripheral fatigue did not occur in the control group. However, the JHS group showed central fatigue. MEP amplitude increased in the JHS group during the fatiguing protocol ($p < 0.01$) before recovering. Superimposed twitch amplitude increased in the JHS group during the fatiguing protocol and stayed elevated during the recovery phase ($p < 0.04$). Time to peak (TTP) amplitude of the torque generated by the TMS was longer in the JHS group ($p < 0.05$). RMS during MVCs decreased during the fatiguing protocol reaching significance during the recovery phase ($p < 0.01$).
Conclusion: JHS participants suffered central but not peripheral fatigue. A modified strength programme to target this is discussed.

1. Introduction

Joint Hypermobility Syndrome (JHS) is an inherited disorder of connective tissue. Although the incidence of JHS in the general population is thought to be low, it is high within National Health Service musculoskeletal services. In fact the incidence of JHS has been reported to be as high as 30% of people referred to a British musculoskeletal triage clinic, 39% of a British pain clinic and 45% of people referred to a British general rheumatology clinic (Connelly et al., 2014; Grahame and Hakim, 2004; To et al., 2016). Up until now, JHS has been classified using the Brighton Criteria (Grahame et al., 2000) however, recently these criteria and the name of the condition has changed to ensure that the spectrum of hypermobility is recognised (Castori et al., 2017). These new criteria are split between Hypermobility Spectrum Disorder and hypermobile Ehlers Danlos Syndrome, which has stricter criteria. However, as this investigation was carried out before the new criteria were published, the term JHS has been used here. Whatever the method of classification and label, the common feature is joint pain and instability but as this is a disorder of collagen that occurs throughout the body it also has features such as varicose veins, uterine or rectal prolapse and hernias (Beighton and Horan, 1969; Birrell et al., 1994; Bravo and Wolff, 2006). More surprising characteristics such as disturbances to pain perception, anxiety, and osteoporosis are also seen (Clark et al., 2011; Grahame et al., 2000; Hakim and Grahame, 2004; Larsson et al., 1993; Mathias et al., 2012). Returning to the physical features, people suffer with chronic long-standing joint pain, subluxations, dislocations, sprains, clumsiness and problems with activities ranging from high level sport and performance to even simple writing tasks (Murray et al., 2013).

It has been reported that up to eighty-six percent of people with JHS suffer with fatigue (Castori et al., 2012; Rombaut et al., 2010; Voermans et al., 2011; Voermans and Knoop, 2011). However, fatigue is commonly overlooked as it does not feature in either the new or former classification criteria (De Wandele et al., 2013; Castori et al., 2017). It has been described as overwhelming, causing psychological distress and can have a bigger impact than pain on daily function (Voermans et al., 2010). In people with JHS, fatigue has been reported to result in malaise, sleep disturbances, poor concentration and memory, poor self-efficacy and self-worth, a change to the person's role in society, anxiety and depression (Castori et al., 2012; Voermans et al.,

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2010)

Little is known about the mechanisms that drive fatigue in this cohort. It is likely to be a multi-faceted problem involving both psychological and physiological aspects. Some aspects of the psychological contribution to fatigue have been explored in a survey of hypermobile people. This established relationship between fatigue and some measures of psychosocial function such as social interaction and ability to concentrate (Voermans et al., 2010). However, no investigations of the physiological contribution to fatigue have been explored. It is perhaps surprising that although Castori et al. (2012), when advising on treatment for fatigue in hypermobile people suggested that fatigue was related to "Central Nervous System fatigue", no study has been undertaken to date to investigate this. Therefore, the objective of this investigation is to focus upon people who suffer with fatigue and have JHS and examine the physiological contribution of central and peripheral fatigue. That is, the inability to maintain muscle output during a fatiguing muscle contraction that might originate from altered central nervous system drive (central fatigue) or inability of the muscle to generate a sustained contraction (peripheral fatigue). Commonly, central and peripheral fatigue are explored using a twitch interpolation method together with recordings of surface electromyographic activity (Merton, 1954). This has been explored in a number of healthy muscles (Sidhu et al., 2009; Todd et al., 2003; Lagan et al., 2008) as well as in pathological conditions such as low back pain (Chiou et al., 2014; Chiou et al., 2015). Exploration of the physiological contribution to fatigue is important as targeted rehabilitation programmes need to be designed in order to focus upon the physiological mechanisms rather than clinicians relying upon clinical experience alone.

2. Method

With ethical approval from the London-Queen Square Research Ethics Committee and written informed consent, two groups of participants were recruited; one control group of healthy participants with normal flexibility and another group of people who were classified as having JHS and complained of fatigue. As there are no previous investigations of voluntary activation in people with JHS, rather than determine the sample size from data gathered from a cohort of patients who have suffered a neurological insult or a healthy cohort alone, we derived the sample size from our previous work using the difference in superimposed twitches between low back pain patients and healthy controls (Chiou et al., 2014). With a difference of 15% and a standard deviation of 11%, and with a power of 0.8 ($p = 0.05$), a sample size of 12 subjects in each group was determined. To recruit participants with JHS, advertisements were placed with two support groups asking for volunteers who suffered with fatigue; Ehlers-Danlos support UK (www.ehlers-danlos.org) and the Hypermobility Syndromes Association (hypermobility.org) as well as placing advertisements within a large London NHS hospital and university. The control participants were recruited by placing advertisements asking for healthy volunteers within the same hospital and university.

Inclusion criteria for the JHS participants were that they scored 4 or more out of 9 on the Beighton scale and fulfilled the Brighton Criteria (Grahame et al., 2000). The Beighton scale gives a score out of 9 for hyperflexibility of joints. The Brighton criteria have major and minor criteria such as multiple joint pain, hypermobility and joint instability. As the Brighton Criteria does not include questions relating to fatigue, all the participants were also assessed using the Fatigue Severity Scale (FSS, Learmonth et al., 2013) and the Multidimensional Assessment of Fatigue scale (MAF, American College of Rheumatology 2017) These questionnaires measure different components of fatigue that include motivation, impact upon physical function and interference upon work, family and social life. Level of activity was assessed using the International Physical Activity Questionnaire (IPAQ, Craig et al., 2003). The inclusion criteria for the control group were that they were healthy, scored 3 or less out of 9 on the Beighton scale, did not fulfil the Brighton criteria and did not suffer with fatigue. Exclusion criteria for the control group were musculoskeletal problems during the previous two years for which they sought treatment. All participants were excluded if they had any medical or neurological conditions. Specifically, people were excluded from the study if they had history of head trauma with concussion or associated loss of consciousness, any neurological problems (e.g. epilepsy, convulsions, seizures or fainting spells), metal implants such as surgical clips, implanted neurostimulators, cochlear implants or pacemaker; as well as currently taking any neuromodulatory medication such as neuropathic pain medication (Rossi et al., 2011).

Age, height, weight, sex and ethnic origin were collected. Arm dominance was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971). Each subject was asked if they were in any pain at any site and to rate it on a visual analogue scale. Subjects were excluded if they suffered with any arm pain on the side to be tested. Pain provocation was assessed regularly during the protocol in order to ensure no pain was provoked. Subjects with JHS also completed the Bristol Impact of Hypermobility questionnaire (Palmer et al., 2016).

Transcranial Magnetic Stimulation (TMS) was delivered during a Maximum Voluntary Contraction (MVC) to investigate central fatigue. Electrical stimulation to the musculocutanious nerve was delivered at rest to explore peripheral fatigue. To achieve this, subjects were seated and the height of the seat varied such that the scapula and the glenohumeral joint were in the anatomical position, the elbow was positioned at 90° flexion and the forearm in supination resting on a table. A strap attached to a calibrated linear strain-gauge transducer was placed just proximal to the wrist crease. Calibration had been carried out at the start of the study using weights incrementally up to 36 kg.

Electromyographic activity (EMG) of the dominant biceps brachii and triceps brachii muscles was recorded using a pair of surface electrodes; one channel per muscle group (Ambu Blue sensor Q Q-10-A/25, www.ambu.com; inter electrode distance 2cms) positioned according to SENIAM recommendations. Electrode placement was checked by the voluntary contraction of the muscles. The data were amplified (NL844, Digitimer UK), filtered (NL125, Digitimer UK) between 30 Hz and 6 kHz, digitised at 4 kHz (1401, Cambridge Electronic Design (CED), UK) and analysed using both Spike and Signal software (CED, UK).

First the subjects performed 3 brief (~3s) maximum voluntary contractions (MVC) of biceps brachii with verbal encouragement. The average amplitude of the torque from 3 MVCs was used to calculate 25% MVC and 50% MVC of torque.

The intensity of the electrical and magnetic stimulation needed to evoke a biceps brachii maximum motor response (MMax) and maximum MEP amplitude (MEPmax) respectively was then determined in the following manner.

Electrical stimulation: a single, square wave pulse of 1 ms duration (constant current stimulator, model DS7A, Digitimer, UK) was delivered to the musculocutaneous nerve using an anode (a flat rectangular gel covered plate) placed on the skin at the level of the attachment of biceps and a roving, damp, gauze covered cathode placed on the skin over the musculocutaneous nerve at the proximal, medial arm. The correct positioning of the cathode was confirmed by visual inspection of the biceps brachii EMG in the absence of a triceps brachii response. With the subject at rest, the stimulation intensity was incrementally increased until the amplitude of the motor response (M) of biceps brachii plateaued. The stimulation intensity to evoke a maximum M (Mmax) was recorded.

Transcranial Magnetic Stimulation: First, the vertex upon the skull was determined by marking the point of transection of a line between each tragus and a line between the nasion and inion. A circular coil (90 mm) from a magnetic stimulator (Magstim200^2, Magstim, UK) was then positioned over the vertex with the coil oriented to induce current in the brain flowing in an appropriate direction to preferentially activate the left motor cortex. Using visual feedback by monitoring torque, the subject was asked to maintain 25% MVC of biceps brachii. TMS was then delivered and incrementally increased until the stimulus required

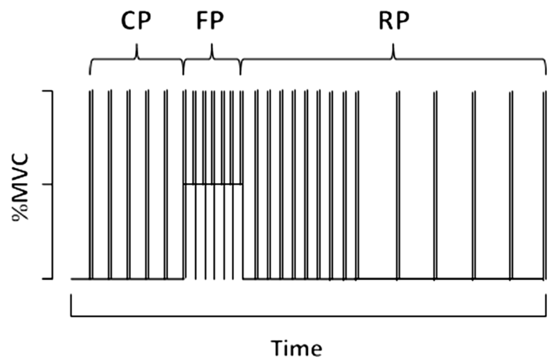

Fig. 1. Schematic representing the timing of evoked responses during the control phase (CP), fatiguing phase (FP) and recovery phase (RP). The 3 min CP was interspersed with TMS at 100% maximum voluntary contraction (MVC), immediately followed by electrical stimulation with the muscle at rest every 30 s. The 2 min FP was interspersed with TMS at 100% maximum voluntary contraction (MVC), immediately followed by electrical stimulation with the muscle at rest every 15 s. After the stimuli, the participant continued the sustained contraction of biceps at 50% MVC. Finally the 8 min RF was interspersed with TMS at 100% maximum voluntary contraction (MVC), immediately followed by electrical stimulation with the muscle at rest every 20 s for 3 min, and then every minute for the final 5 min.

to evoke a maximum amplitude Motor Evoked Potential (MEPmax) was reached and the stimulus intensity (percentage maximum stimulator output) was recorded.

Protocol: A control phase, a fatiguing phase and a recovery phase were carried out sequentially (see Fig. 1). A verbal Borg scale (0–10) to assess level of exertion was collected at the start of the control phase, before and immediately after the fatiguing phase and at the end of the recovery phase (Borg and Kaijser, 2006).

Control phase: Every 30 s for 3 min, a brief MVC of biceps brachii was performed during which a stimulus from the TMS was delivered. This was immediately followed by an electrical stimulus to evoke Mmax with the biceps brachii at rest. As explained earlier, the TMS delivered during an MVC was used to investigate central fatigue. The electrical stimulation delivered at rest was used to explore peripheral fatigue.

Fatiguing phase: The subject was asked to sustain a contraction of the biceps brachii at 50% MVC for 2 min. This was assisted by using the visual feedback of the torque upon a target line on a monitor as well as verbal prompts. This short fatiguing protocol was chosen after piloting fatiguing contractions with JHS sufferers to ensure that people with JHS could complete the protocol and yet felt fatigued by the task. Longer contractions at lower intensity, which have been used in other investigations of fatigue in healthy subjects (Sogaard et al., 2006), were not attainable by the JHS cohort during this pilot. Stimuli were delivered, as in the control phase, but repeated every 15 s for 2 min with the subject instructed to return to 50% MVC between stimuli.

Recovery phase: The control phase protocol was repeated every 20 s for 3 min, and then every minute for a further 8 min.

Data analysis: Peak to peak amplitudes of the M responses and MEPs were also recorded and normalised to the amplitude of the M response or first MEP of the fatiguing protocol. Root mean square (RMS) amplitude of the EMG taken in 50 ms prior to the TMS pulse, whilst the subject was contracting at MVC was normalised to the average of the initial brief MVCs. Twitches evoked from TMS and electrical stimulation were identified using a custom-made script. The twitch amplitudes were calculated as the difference between the mean voluntary torque level in 50 ms prior to the stimulus and the maximum torque level obtained during the twitch. The time-to-peak (TTP) amplitude of the twitches was also recorded using data from the TMS pulse as well as the electrical stimulation.

Statistical analysis: Data were analysed using SigmaPlot (Systat Software, USA). Demographic data were described as mean ± standard deviation and compared between the control group and the JHS group using independent t-tests for numerical data (age, height, weight), Friedman repeated measures ANOVA on ranks for ordinal data over time (Borg Scale), Mann Whitney U tests for categorical data between groups (Beighton scale, fatigue data, BIHQ and IPAQ) and the Chi square test to assess for gender differences. After testing for the normal distribution of the data using Shapiro Wilk test, 2 way ANOVAs were used to compare across time and between groups, testing for differences in torque, MEP amplitude, M amplitude, RMS, TTP amplitude from the TMS and electrical stimulation, superimposed twitch (SIT) and resting twitch (RT). Significant differences have been reported over the time course of the protocol, and between groups. Statistical significance was set at $p < 0.05$ and Bonferroni corrections were applied to allow for multiple comparisons if differences were seen. The data are presented as mean ± standard deviation in the text and mean ± standard error of the mean in the figures.

3. Results

The demographic data are described in Table 1. Statistical tests revealed that gender, age, height and activity did not differ between groups. However, other markers of fatigue, flexibility and pain (felt outside the upper limb) did differ ($p < 0.05$).

The Borg Scale (see Fig. 2) revealed that both groups' perception of fatigue changed over time ($p < 0.001$) and differed in intensity between the groups ($p < 0.02$). Post hoc tests revealed that the difference between groups was during both the fatigue ($p = 0.02$) and recovery phase ($p = 0.001$). Over time, the JHS group felt increasing fatigue, that was a clinically meaningful increase after the control phase of the protocol alone reaching 3.2 ± 2.2/10 at the start of the fatiguing contraction ($p = 0.05$); this is equivalent to a perception of exercising at a "moderate" level (Borg 1982). This rose to 6.5 ± 1.5/10 at the end of the fatiguing contraction ($p = 0.05$) remaining at 6.8 ± 2.8/10 even after the recovery phase; this is the equivalent to a perception of exercising at a "very strong" level (Borg 1982). Over time, the control group felt fatigued by the sustained contraction (4.0 ± 2.7/10; $p = 0.05$), however this seemed to begin to reduce during the recovery phase (2.1 ± 1.7/10).

There was no difference in the superimposed twitch amplitude between groups ($F_1 = 2.74$; $p = 0.11$; see Fig. 2). There were changes over time ($F_{27} = 3.23$, $p < 0.001$) with no significant interaction ($F_{27} = 1.39$, $p = 0.10$). In the JHS group it increased during the fatiguing protocol and stayed elevated during the recovery phase ($p < 0.04$). This was not the case for the control group where the superimposed twitch remained stable over time ($p = 1$).

There were no differences in torque normalised to MVC between groups ($F_1 = 2.01$, $p = 0.16$). In addition, the normalised torque did

Table 1
Demographic data of height, weight, sex, Beighton score, Fatigue Severity Score (FSS), multidimensional assessment of fatigue scale (MAF), pain severity using a visual analogue scale (VAS), Bristol impact of Hypermobility (BIoH) and international physical activity questionnaire (IPAQ). Data is presented as mean ± standard deviation. * denotes significance at $p < 0.05$.

	Age	Height	Weight	Sex (% women)	Beighton score	FSS	MAF	VAS	BIoH	IPAQ
Control	37.4 ± 8.2	168.8 ± 10.2	63.5 ± 12.3	75.0	1.5 ± 1.5	8.9 ± 12.6	13.1 ± 9.0	0.1 ± 0.3		4863.1 ± 2474.4
JHS	37.0 ± 8.5	170.9 ± 5.7	*75.2 ± 13.7	91.7	*7.1 ± 1.4	*47.0 ± 8.8	*32.7 ± 11.7	*4.0 ± 2.2	194.5 ± 66.8	4169.9 ± 3707.1

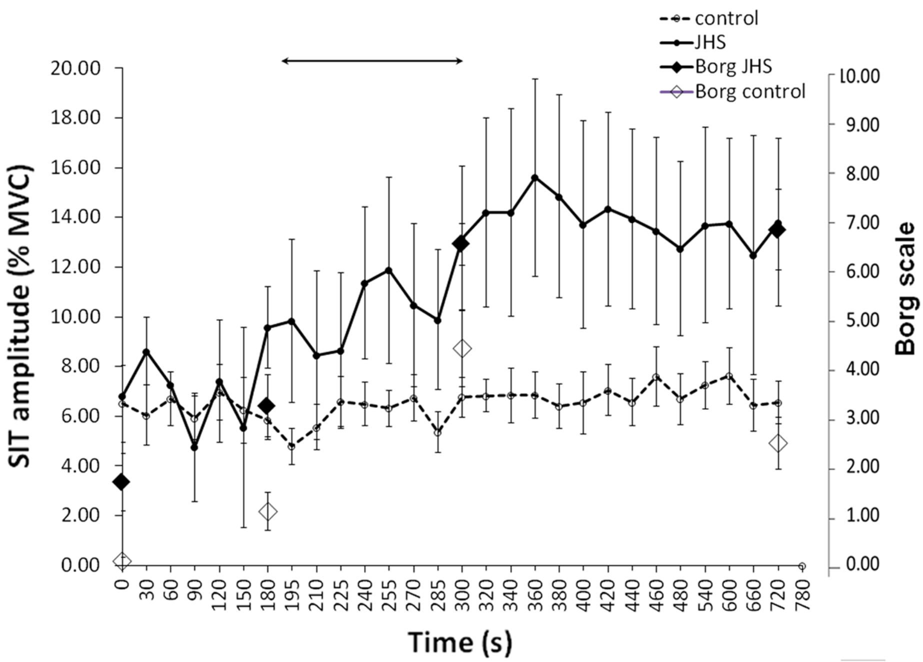

Fig. 2. The left axis represents the mean ± standard error of the mean of the superimposed twitch (SIT) amplitude as a percentage of maximum voluntary activity (MVC) for the control group (open diamonds) and joint hypermobility syndrome group (JHS; closed diamonds). The right axis represents the mean ± standard deviation of the Borg scale, which is a function of their perceived level of fatigue. The horizontal axis represents time in seconds (s). The horizontal double headed arrow represents the duration of the fatiguing protocol.

not change over time ($F_{27} = 0.84$, $p = 0.71$).

There was no difference in MEP amplitude between groups ($F_1 = 0.43$, $p = 0.52$; see Fig. 3). There were changes over time ($F_{27} = 2.17$, $p < 0.01$) with no significant interaction ($F_{27} = 0.8$, $p = 0.75$). In the JHS group the MEP amplitude increased immediately during the fatiguing protocol returning to baseline in the recovery phase ($p < 0.01$; see Fig. 3). This was not the case for the control group where MEP amplitude remained stable over time ($p = 0.88$).

The time to peak (TTP) amplitude of the torque generated by the TMS differed between groups ($F_1 = 5.4$, $p < 0.03$; see Fig. 4) with the TTP amplitude longer in the JHS group. This TTP amplitude difference between groups occurs during the fatiguing protocol and remained longer during the recovery phase ($F_{27} = 1.5$, $p < 0.05$). The TTP amplitude did not change over time ($p = 0.06$). There was no significant interaction between group and time ($F_{27} = 0.94$, $p = 0.56$).

The amplitude of Mmax did not differ between groups ($F_1 = 0.4$, $p = 0.55$) or change over time ($F_{27} = 0.8$, $p = 0.77$).

The normalised RMS recorded during the MVCs did not differ between groups ($F_1 = 3.5$, $p = 0.08$; see Fig. 5). However, RMS during the MVCs did differ over time ($F_{27} = 10.2$, $p < 0.001$). In the JHS group, RMS declined and became significantly lower during the recovery period ($p < 0.01$). This was not the case for the control group, where RMS remained largely unchanged over time. There was significant interaction between group and time ($F_{27} = 1.58$, $p = 0.03$).

The resting twitch (RT) size did not differ between groups ($F_1 = 0.9$, $p = 0.34$). RT size did differ over time ($F_{27} = 5.0$, $p < 0.01$; see Fig. 6) but there was no significant interaction ($F_{27} = 1.25 p = 0.18$). In the JHS group, the RT size increased in amplitude during the fatiguing protocol ($p < 0.02$); returning to baseline in the recovery phase; this was not the case for the control group, which remained stable over

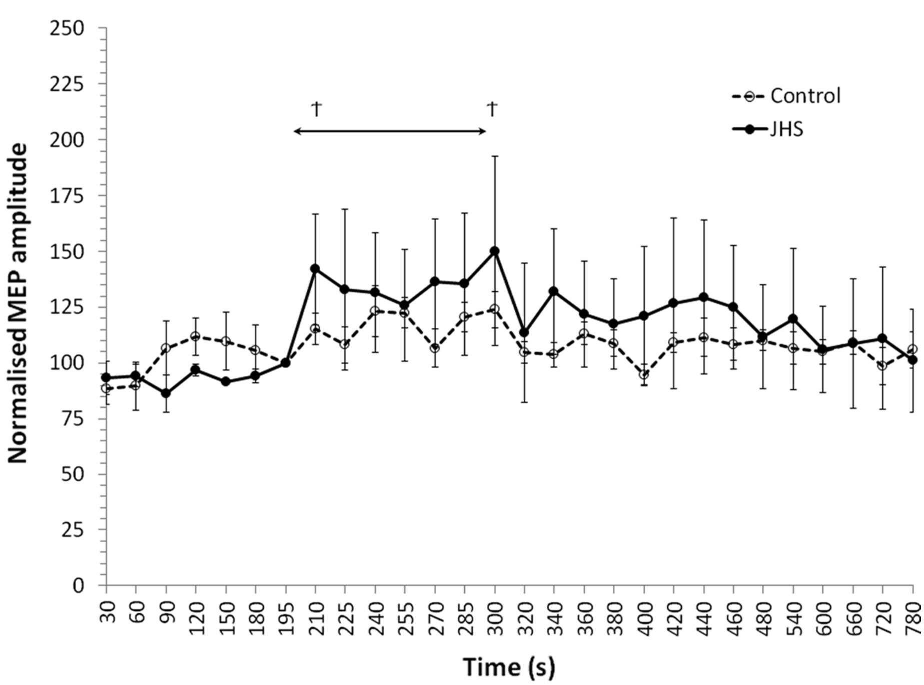

Fig. 3. The y-axis represents the mean ± standard error of the mean of MEP amplitude normalised to the first MEP amplitude of the fatiguing protocol, for the control group (open circles) and joint hypermobility syndrome group (JHS; closed circles). The horizontal double headed arrow represents the duration of the fatiguing protocol. The † represents within JHS group significant differences.

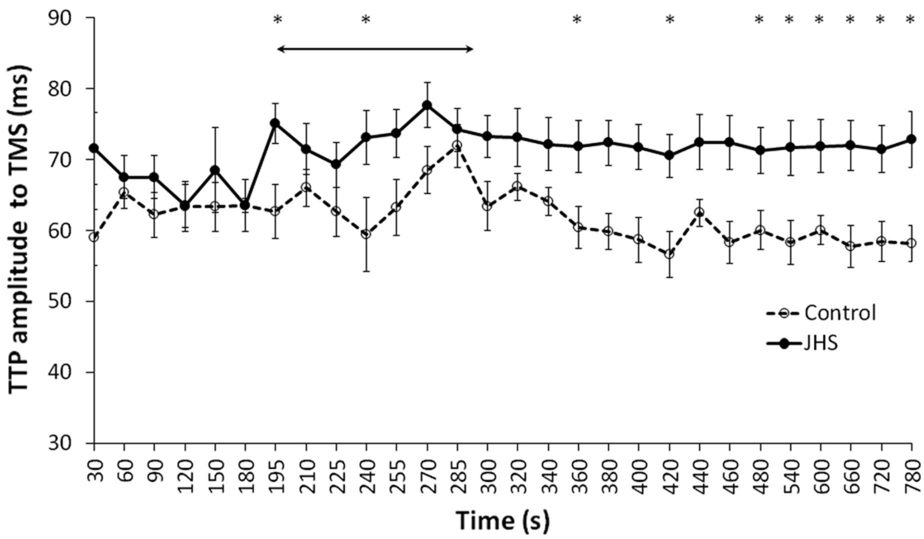

Fig. 4. The y-axis represents the mean ± standard error of the mean of the time to peak (TTP) torque generated by the TMS for the control group (open circles) and joint hypermobility syndrome group (JHS; closed circles). The horizontal double headed arrow represents the duration of the fatiguing protocol. The * represents between group significant differences.

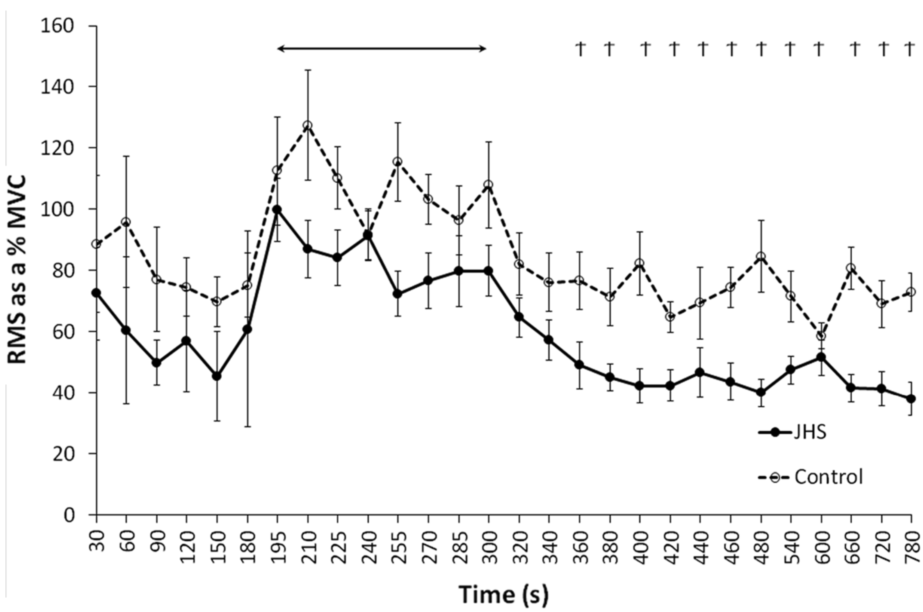

Fig. 5. The y-axis represents the mean ± standard error of the mean of the normalised RMS generated during a Maximum Voluntary Contraction (MVC) for the control group (open circles) and joint hypermobility syndrome group (JHS; closed circles). The horizontal double headed arrow represents the duration of the fatiguing protocol. The † represents within JHS group significant differences.

time. The TTP amplitude of the resting twitch did not differ between groups ($F_1 = 2.06$, $p = 0.17$) or over time ($F_{27} = 0.56$, $p = 0.97$).

4. Discussion

This is the first investigation of central and peripheral fatigue in JHS individuals who suffer with fatigue. Using a short period and low intensity fatiguing protocol compared to other investigations of musculoskeletal cohorts, this JHS group felt greater fatigue than the control group and this perception of fatigue did not return to baseline after an 8 min recovery phase.

The results from the JHS group suggest central fatigue, which did not occur in the control group. This is evidenced by the increased amplitude of the superimposed twitch, illustrating that the TMS was able to evoke an increase in torque which was not possible to obtain voluntarily (Cheng et al., 2013). This result does not give an indication about why or from where this central fatigue originates but it separates the JHS group from the healthy controls. Recently, Kuppuswamy (2017) suggested that people's perception of fatigue during movement may be driven by alterations in sensory input into the central nervous system. Where afferent information is accurately delivered for precise movement, then perception of effort is low. However, when sensory information needs to be attended to by the central nervous system, perceived effort is high (Kuppuswamy, 2017). This proposal is interesting as people with JHS have poor proprioception (Fatoye et al., 2008; Mallik et al., 1994; Smith et al., 2013). This sensory deficit may lead to changes in descending control (Komori et al., 1992) as well as higher perceptions of effort (Kuppuswamy, 2017).

As would be expected with generation of fatigue, the MEP amplitude increased during the fatiguing protocol in the JHS group, and again this did not occur in the control group. Such increases have been found previously with a fatiguing protocol and are thought to reflect mechanisms which help to overcome inhibition in order to maintain function (Benwell et al., 2007). Once again this demonstrates a separation of the JHS group from the controls.

The TTP amplitude of the twitch generated by the TMS was longer in the JHS group. This suggests that the JHS cohort may be recruiting motor units differently or have selective loss of the faster motor units. With an MVC, motor units are recruited following Henneman's size principle, that is, slow motor units are recruited before the faster units whilst the force is generated (Mendell, 2005). The result here might suggest that the fast motor units and therefore the faster twitch fibres

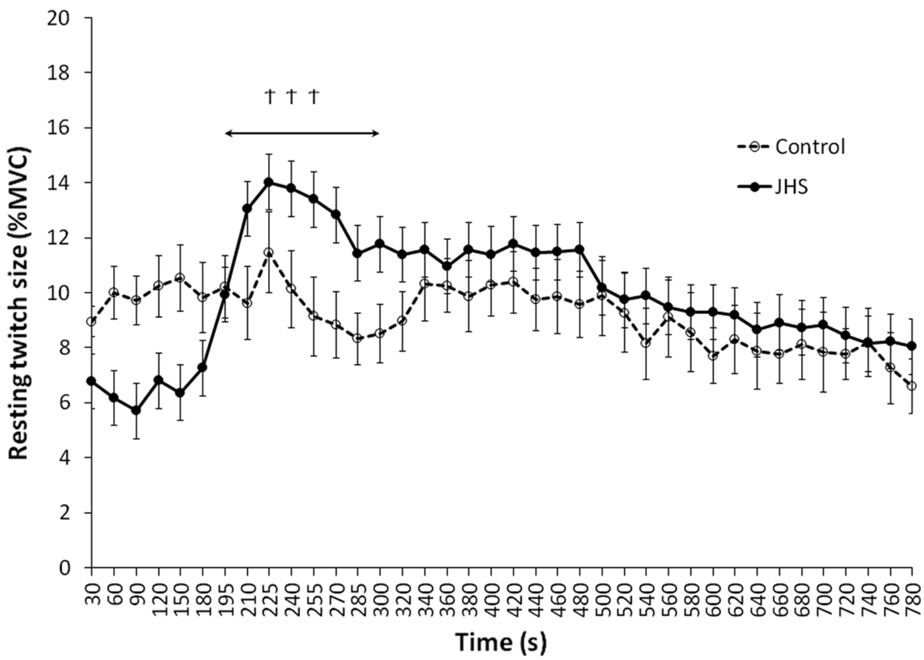

Fig. 6. The y-axis represents the mean ± standard error of the mean of the resting twitch amplitude for the control group (open circles) and joint hypermobility syndrome group (JHS; closed circles). The horizontal double headed arrow represents the duration of the fatiguing protocol. The † represents within JHS group significant differences.

are not being recruited in the same way as the control group resulting in a slower generation of the maximum twitch. This is interesting as selective type II fibre loss has been seen with both pain related disuse and as well as a sedentary lifestyle alongside aging (Fink et al., 2007; St-Jean-Pelletier et al., 2017). It should be noted however, that the TTP amplitude generated at rest by electrical stimulation of the peripheral nerve did not reveal the same difference between groups. This therefore suggests that the fibre type composition may be the same as the control group, whereas the drive from the CNS during voluntary contractions differs such that type I fibres are being preferentially recruited.

The more surprising results lie in the investigation of peripheral fatigue. Here the resting twitch increased in the JHS group where as one would expect it to decrease in amplitude with fatigue. One explanation could be that the JHS group received inconsistent intensity of the electrical stimulus. However, the stability of the M response in both groups discounts any methodological error. Instead, an alternative explanation could be related to the task. The JHS group rarely perform maximum voluntary contractions during everyday tasks as they may be wary of provoking pain (Rombaut et al., 2015; Scheper et al., 2015). Here, the increase in resting twitch during the fatiguing protocol is consistent with an improvement in the muscle's capacity to generate torque. This could relate to the effect of repeated contractions of an untrained muscle akin to the increase in resting twitch size immediately following a maximum contraction; the potentiated twitch (Kufel et al., 2002). Although the ability of the muscle to generate torque may have increased, the EMG activity during the intermittent MVCs did not increase. In fact, the RMS during MVCs decreased during the fatiguing protocol, reaching significance in the recovery phase. A decrease in the EMG during MVCs superimposed upon a sustained contraction has been previously reported (Sogaard et al., 2006) substantiating the notion that the protocol induced central rather than peripheral fatigue in the JHS group.

Central fatigue is reduced in response to exercise in healthy people (O'Leary et al., 2017; Triscott et al., 2008). It is interesting to note that O'Leary found higher intensity interval training reduced central fatigue whereas the same work done using lower intensity exercise delivered over a longer, continuous exercise bout did not have the same impact. This approach might be useful since the JHS group exhibit central fatigue. However, although high intensity interval training was effective for a healthy cohort, it is likely that a JHS cohort in pain would require a paced increase to achieve this intensity to allow them to grow in confidence and therefore achieve and adhere to high intensity exercise. Reducing central fatigue may lead to reduced symptoms and improvements in function.

Declaration of Competing Interest

Interests to declare: MT held a Pre doctoral fellowship from the Imperial Health Charity and CMA held a Senior Clinical Lectureship from the National Institute for Health Research.

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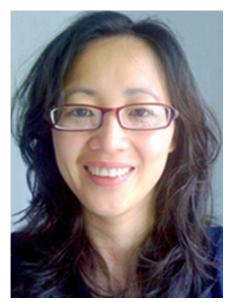

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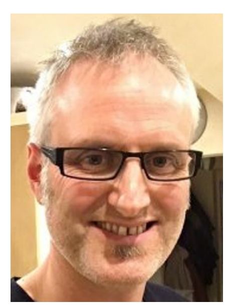

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